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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,821	12/21/2000	Daniel C. Carter	P06896US00/BAS	6567

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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	5

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/740,821	Applicant(s) CARTER, DANIEL C.	
	Examiner Samuel W Liu	Art Unit 1653	

-- The MAILING DATE of this communication appears on th cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *13 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14,15 and 17-20* is/are rejected.

7)☒ Claim(s) *4 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

"DTAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-12, 14-15 and 17-20 filed 6 May 2002 (paper NO:3) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). In view of Applicants' election, Claims 13 and 16 are withdrawn from consideration as directed to non-elected invention. Therefore, the elected Claims 1-12, 14-15 and 17-20 are examined in this Office Action.

Objection to Claims

The disclosure is objected to because of the following informalities:

(1) In Claim 4, "n-terminal" should be changed to "N-terminal". The same are Claims 5 and 20. Also, in Claim 4, "a one-amino acid truncation" should be changed to "one-amino acid truncation", alternatively, to "an one-amino acid truncation".

(2) In Claim 5 "affinity to trace metal" should be changed to "affinity for trace metal".

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 15 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for unmodified albumin-based composition, does not

reasonably provide enablement for the composition based on a bio-engineered human serum albumin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly concerned, to make and use the commensurate in scope with these claims.

There are genus claims. Claims 4 and 5 recite "at least one-amino acid truncation (deletion) at N-terminal region of the albumin". The claims introduce variants, which are unpredictable absent the factual indicia to the contrary.

Applicants are in possession of cosmetological composition based on unmodified human serum albumin, but not in the possession of the composition based on bio-engineering generated human serum albumin. The instant application provides no working example and guidance for making the composition thereof. The present application describes only preparation of the unmodified albumin-containing cosmetological composition; the skilled artisan cannot envision all the contemplated amino acid sequence possibilities (variants of engineered albumin) and possible use in cosmetology or dermatology. Thus, adequate written description requires more than a mere statement that it is part of invention. The sequences themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1610, 1606 (CAFC1993). The Guideline for the Examination of Patent Application Under the 35 U.S.C. 112 the first paragraph "written description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e. structure or other biochemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in

possession of the genus (Federal register, Vol. 66, NO. 4, page 1099-1111, Friday January 5, 2001, see especially page 1106 the third column). The specification disclosure is insufficient to enable,skilled artisan to practice the invention as broadly claimed without an undue amount of experimentation. Thus, Applicants were not in possession of the claimed genus at the time the invention was made.

In this regards, the application disclosure and claims have been compared per the factors indicated in the decision *in re* Wands 8 USPQ2d 1400, 1400 (Fed. Cir. 1998) as to undue experimentation. The factors include: 1) the nature of the invention; 2) the breath of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

(1) The scope of the claims:

The current application is directed to a cosmetological or dermatological preparation composed of N-terminal mutated (truncated or deleted) albumin. The specification does not provide guidance and working examples for this preparation and for how to generate mutant proteins. There are numerous unpredictable mutant variants within the scope of the claims associated with the preparation but which are not enable.

(2) The nature of the invention:

The claimed composition is directed to engineering the albumin that is an essential component for the claimed cosmetological composition. The claims encompass numerous structural variants; none have been described in the specification nor in the claims. Many structural variants would be inactive and/or unpredictably inactive in the absence of factual indicia to the contrary.

The specification of the application does not describe relationships between the structural variation at N-terminus of the albumin and cosmetological activity and between the structural variation at N-terminus of the albumin and albumin's affinity for the binding region VI of the protein.

In consideration of the above the specification does not demonstrate possession and enablement for (***a***) the N-terminal modified albumin protein; (***b***) a biologically active mutant or composition; and (***c***) any preparation comprising any polypeptide of the foregoing (***a***) and (***b***).

There is no guidance in the specification and claims as to which amino acid residue(s) within the polypeptide can be substituted and/or deleted, and whether the resulting polypeptide would retain the biological function. Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). Given the lack of sufficient guidance and working examples, predicting what changes can be made to N-terminus of the albumin that after deletion will retain the desired folding structure is unpredictable.

(3) The state of the prior art:

The general knowledge and level of skilled in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attribute and characteristics that identify a biological active fragment for its use, one of skilled artisan is require performing undue experimentation in order to screen, identify and isolate appropriate folded albumin, especially the binding region VI, provided that the region VI is attributed to the cosmetological or dermatological activity of the engineered human albumin protein.

Since the disclosure fails to describe the consequence of the structural variation at N-terminus of the albumin, the specification needs to provide sufficient guidance and working examples to support enabling.

(4) The quantity of experimentation necessary:

In the absence of working examples with regard to the above mentioned numerous variant sequences, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trial and error, i.e. experimentation to practice the claimed invention. One of the skilled artisans would be required to carry out a large body of tests for which truncation of an N-terminal region of the albumin are applicable to cosmetic or dermatological utilization.

(5) The unpredictability of the art:

Because of the claimed variants with regard to truncation (deletion) at N-terminal region of the protein are highly variant (see the foregoing statement), the invention is unpredictable in the absence of factual indicia to the contrary. As shown by Petersen, C. E. et al (*Biochemistry* (1997) Vol. 36, 7012-7017), a point mutation can sufficiently change biochemical activity.

(6) The relative skill of those in the art:

The general knowledge and level of skill in the art do not supplement the omitted description with respect to the human albumin variants with unpredictable folding structures. In view of the preceding factors (1-5), the level of skill in this art is high and requires at least a biochemist at Ph.D. level with several years of experience in molecular biology and dermatology; yet, even with that level of skill in the art, predictability of the results is still highly variable.

Petersen, C. E. et al has shown that a single amino acid alteration cause a change at human serum albumin thyroxine binding subdomain and thereby a dramatic alteration [2 order of magnitude] of the albumin's affinity for the ligand (see Petersen, C. E. et al (1997) *Biochemistry* Vol. 36, 7012-7017).

In consideration of each of factors stated above, there is undue experimentation because of variability in prediction of outcome that is not addressed by the instant application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 14-15 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 9 are rejected as indefinite under USC 112 the second paragraph because the claims depend from themselves for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. In addition, claims 7 and 9 which depend from theses claims are also indefinite.

Claim 1 is indefinite in the recitation "other beneficial cosmetics or dermatological purpose"; what is the said beneficial purpose? The claim is also unclear as to what is "a suitable" products for cleaning, conditioning, cosmetic or dermatological product. Claim 14 is indefinite for the same reason as stated above. Dependent claims are also rejected.

Claim 4 is indefinite because the recitation "at least a one-amino acid truncation" is unclear as to how many one-amino acid truncations are necessary and sufficient for steric barrier to the region VI of the albumin because the term "at least" sets no upper limit to mutagenesis of albumin N-terminus. If there are amino acids (≥ 2) subject to truncation mutagenesis, then, whether or not these one-amino acid truncations are clustered together or scatter within N-terminal region of human serum albumin. Further, given other types of truncations, it is not clear as to whether or not multiple amino acid truncations are applicable. Claim 5 is indefinite for the same reasons in the foregoing statement.

Claim 5 is indefinite in (i) the recitation "the binding region VI"; where and what the binding region VI is regarded to; (ii) the recitation "trace metals"; it is not apparent as to whether it refers to as the metals that are essential to animal nutrition in trace concentration or refers to trace amount of the said metals; (iii) the recitation "sufficient to cause" which is not apparent regarding to what extent the peptide truncation would cause satiric hindrance; and (iv) the

recitation "reduce or eliminate"; it is not apparent as to which effect, eliminate or reduce, on the albumin's affinity for the metals is caused by satiric barrier in the region VI of the protein because there is significant difference between reduction and elimination. Claim 20 is indefinite for the same reasons in the foregoing statement.

Claim 11 is indefinite because "in the range about 1 to 250 mg/ml" leaves room to exceed 250 mg/ml and because it is ambiguous regarding what are encompassed in this limitation. The recitation appears to set "±" parameter on the both ends of the concentration range. Claim 12 is unclear for the similar reason.

Claim 17 is indefinite because a range of concentration of serum albumin falls into in an ambiguous range of glycerin solution. What is the glycerin solution therein? Does the solution contain other solute(s) other than the albumin protein or is the said solution consists of albumin protein and glycerin? Claim 17 would be clear if the claim is rewritten as, for example, "1-60 mg/ml human serum albumin dissolved in glycerin solution".

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The claims 1-2, 6-12, 14 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kligman, A. M. (EP 0244859, 1987).

Claims 1-2 and 6-7 of the instant application set forth a composition dissolved in a liquid soap for cosmetically treating skin in form of cream. This has been anticipated by Claims 1 and 9 of the Patent EP 0244859 which claims disclose a liquid composition suitable for treating human facial skin to prevent wrinkle and smoothing of the skin.

Claims 7-12 of the instant application disclose the serum albumin of the composition is dissolved in a glycerin solution with specific concentrations: 10-60% (Claim 9), 15% (Claim10), in the range of about 1-250 mg/ml (claim 11) and about 40 mg/ml (Claim 12). The reference Patent (EP 0244859) anticipate the same because Claim 8 of the reference Patent, which read on Claim1, teaches use of glycerine solution for formulating the cosmetical composition that encompasses concentrations of an aqueous carrier (e.g. glycerine) including the concentrations set forth in the claims of the instant application.

Also, Claims 4-5 of the reference Patent, which disclose that the serum albumin is present in an amount in the range of about 5-50% and 10-20% (by weight), respectively, anticipates the concentrations of human serum albumin set forth in Claims 17-19 of the instant application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483.

The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or

703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

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June 17, 2002

Christopher S. F. Low

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